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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/986,750	11/09/2001	Richard M. Pires	0942.5080001/RWE/FRC	5957
26111	7590	11/17/2003	EXAMINER	
STERNE, KESSLER, GOLDSTEIN & FOX PLLC 1100 NEW YORK AVENUE, N.W. WASHINGTON, DC 20005			SCHULTZ, JAMES	
			ART UNIT	PAPER NUMBER

1635

DATE MAILED: 11/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Applicati n No.

09/986,750

Applicant(s)

PIRES ET AL.

Examin r

J. Douglas Schultz

Art Unit

1635

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 9/11/2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
- ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 11 September 2003. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☐ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_

Claim(s) objected to: \_\_\_\_\_

Claim(s) rejected: \_\_\_\_\_

Claim(s) withdrawn from consideration: \_\_\_\_\_

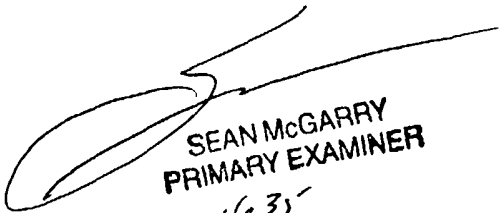
8. ☐ The drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_
10. ☐ Other: \_\_\_\_\_

Continuation of 5. does NOT place the application in condition for allowance because: applicants' arguments that Lyttle et al. teaches away from and therefore cannot be combined with Kempe is not considered convincing. Applicants argument that Lyttle teaches away from Kempe is based on a citation from Lyttle which indicates that "Post synthesis cleavage protocols involve either strongly basic conditions with heating at elevated temperatures with heating at elevated temperatures for long periods, or the use of alkali metal salts which require additional steps for removal. These limitations have, so far, outweighed the added convenience of one support material for every sequence, and prederivatized supports are still predominantly preferred". From this applicants broadly conclude that "[t]he use of strongly basic and harsh reagents was a limitation in the solid phase synthesis of polynucleotides", and that because Kempe's method relies upon the use of ammonia gas which is harsher, that Lyttle thus cannot be combined with Kempe. However, this would not convince one of ordinary skill in the art that the combination of Kempe and Lyttle is untenable, because both of Kempe et al. and Lyttle et al. disclose the use of the relatively "milder agent" ammonium hydroxide as a preferred compound for use in their respective methods. Furthermore, this is the same compound disclosed and claimed for use in applicants' method, and encompassed by applicants' broadest claims. Thus applicants arguments appear to be directed solely to the limitation found in claim 10 drawn to the use of "harsh" ammonia gas, and not relevant to the remainder of the claims. As a side note, applicants are reminded that claims 24 and 25 are not drawn to the use of pressurized ammonia gas as recited in applicants' arguments; in fact, gaseous ammonia is a limitation not found in these claims.

Regarding the use of ammonia gas of claim 10, Lyttle indicates that the limitations of using "harsh" reagents to cleave universal linkers were due not only to the harshness of the compounds, but also to the extra time and extreme temperatures involved, and impurities introduced in these methods of cleaving such universal linkers, which are precisely the problems that Kempe solves by using gaseous ammonia and ammonium hydroxide vapor reagents to significantly reduce cleavage and purification time. Moreover, Lyttle indicates only that the harsh reagents and conditions required to cleave universal linkers have led to other types of linkers being "predominantly preferred". This is a far cry from saying that said harsh conditions cannot work. Accordingly, while it is true that Lyttle discloses the use of the comparatively less harsh ammonium hydroxide, this teaching does not amount to a teaching away. Contrary to applicants' contention, nowhere is it indicated that gaseous ammonia or other harsh reagents would not work in the methods of Lyttle, and Lyttle does not teach that they "should be avoided". For these reasons, the rejection of record is considered to be proper.

Finally, applicants argue that the method of cleaving a universal linker using ammonia gas as claimed in claim 10 is not suggested by the prior art because the ammonia gas is harsher than ammonium hydroxide because ammonia gas does not combine with water as does ammonium hydroxide. However, this fact is in dispute, because the instant method requires the universal support attached to synthesized oligo to be washed in water before ammonia gas cleavage according to standard methods. Thus, it stands to reason that unless the water is removed from the solid support/oligo conjugate and the conjugate dried before cleavage, a step not disclosed by applicants, that water remaining on the conjugate would combine with the gaseous ammonia to create ammonium hydroxide, contrary to applicants stated point of novelty.

No claims are allowed.

  
SEAN MCGARRY  
PRIMARY EXAMINER  
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